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AN AGENT-BASED FRAMEWORK OF TUMOUR HETEROGENEITY

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Abstract. Tumour heterogeneity arises from diverse cell phenotypes with different characteristics. To explain this heterogeneity, the cancer stem cell (CSC) hypothesis suggests that cancer cells are hierarchically organized. The CSCs are at the top of the hierarchy with unlimited proliferative capacity and may undergo symmetric or asymmetric divisions to generate CSCs and non-CSCs (progenitors and mature cells). However, experimental evidence suggests that there is a degree of plasticity between the CSC and non-CSC subpopulations, which is associated with aggressive tumour progression and treatment resistance. Here, we use an agent-based approach for the CSC model with plasticity to study mammosphere formation efficiency and average mammosphere size, as well as the fraction of CSCs. We use our experimental data on breast cancer cell lines to obtain the model parameters and then apply sensitivity analysis to determine the key parameters of the model.

Keywords. Cancer stem cells, tumour heterogeneity, agent-based model, mammosphere formation, cancer plasticity

1 Introduction

In general, every cancer should be treated as a different disease and requires individualized treatment due to several degrees of heterogeneity. Each tumour responds to treatment differently because it has its own population of cells and its own microenvironment. At the level of cells, there are different cell phenotypes even if the cell genotypes are identical [11]. Each phenotype has its own set of characteristics with respect to cell behaviour, such as proliferation and death rate, and may react differently to a given microenvironment [7, 11]. Ideally, these levels of heterogeneity should be taken into account when designing a model of tumour growth and its response to a treatment strategy.

In the traditional view of cancer, known as "clonal evolution", tumour heterogeneity is the result of genetic heterogeneity within a tumour [13]. Cancer is initiated by a series of mutations that allow a cell to overcome the